Although CRC is curable by surgery if detected in the early stages, a large proportion of patients will develop metastatic disease. For many years, 5-fluorouracil (5-FU)-based regimens (usually in combination with folinic acid [FA] [leucovorin]) have been the mainstay of chemotherapy for the treatment of advanced CRC (1). In recent years, a number of newer agents have shown good activity in CRC. One such drug, the topoisomerase I inhibitor irinotecan, is now considered a standard choice in combination with 5-FU/FA in the first-line treatment of advanced disease (2-4) (Table 1). In addition, 5-FU/FA in combination with the third-generation platinum agent, oxaliplatin, has demonstrated improved response rates and progression-free survival (PFS) compared with 5-FU/FA alone (5-7). Results from a phase III crossover study demonstrated that combinations of 5-FU/FA with irinotecan (FOLFIRI) or oxaliplatin (FOLFOX) were similarly effective in terms of response rate, PFS and tolerability, in the first-line treatment of metastatic CRC (8). There is no doubt that treatment regimens introduced in recent years have led to an increase in response rate, and survival now exceeding a median of 20 months in patients with metastatic CRC. However, there is a clear and urgent need for new treatments to improve patient outcome in both the first- and second-line settings.

EGFR and VEGF represent potential targets for novel therapeutic intervention in CRC. The encouraging results from the phase II studies have prompted the initiation of a European two-arm study (the BOND study) (9) which is designed to compare the effects of cetuximab (n=111) with cetuximab plus irinotecan (n=218) in patients with EGFR expressing CRC which have progressed on, or within three months of, irinotecan-based chemotherapy. Patients treated with Cetuximab and Irinotecan had double as high response rate compared to patients receiving Cetuximab alone (23% vs. 11%, p=0.007) and also a significantly longer median time to progression (4.1 vs. 1.5 months, p<0.0001), while the overall survival was not statistically different albeit in favor to the combination treatment (8.6 vs. 6.9 months).

A number of trials have investigated its use in combination with conventional chemotherapy for the first-line treatment of advanced CRC with promising results(10,11).

REFERENCES


